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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/737,350	12/15/2003	Elias Georges	112418-149 and AUR-011US	6000

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/737,350	GEORGES ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-108* is/are pending in the application.

4a) Of the above claim(s) *10-108* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/5/04, 03/22/06*, 10/7/05, 3/16/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on May 5, 2006 is acknowledged. The traversal is on the ground(s) that searching all the claims would not put a serious burden on the examiner, because Groups I, II, X, and XI are directed to similar methods of detecting the level of HSC70 expressed on the cell surface of a test neoplastic cell. The inventions utilize binding agents to detect the expression of cell surface-expressed HSC70 on test neoplastic cells and examination of Groups I, II, X, and XI, and the examination of the claims would require a search for methods utilizing binding agents to detect cell surface-expressed HSC70. For the purposes of the search, it should not matter that the method attempts to detect the presence of a test neoplastic cell or a test multi-drug resistant cell. Regardless of the different objectives of the inventions in Groups I, II, X, and XI, the examination would require a search for binding agents specific for HSC70.

These arguments have been fully considered but found unpersuasive because the claims are not drawn to binding agents to HSC70, and search of binding agents to HSC 70 would not result in whether the protein would be marker for a neoplastic cell has resistant or potential.

As for the species election, search would be expanded if the generic claims are allowable. The requirement is still deemed proper and is therefore made FINAL.

Claims 10-108 are withdrawn as non-elected inventions, there being no allowable generic or linking claim.

Claims 1-108 are pending and Claims 1-9 are examined on the merits.

Information Disclosure Statement

The Information Disclosure Statements filed on 12/15/2004, 3/16/2005, 10/7/2005, and 3/22/2006 has been considered. A signed copy of the 1449 forms is attached hereto.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vitro blood cancer cell lines cells, and breast cancer cell lines cells MDR detection, does not reasonably provide enablement for in vivo MDR detection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-9 are drawn to method for detecting multidrug resistance or multidrug resistance (MDR) potential in a neoplastic test cell (specific neoplastic cells are listed in claims 609, and tissue samples are listed in claim 9) by measuring a level of cell surface-expressed HSC70 and comparing that level in a neoplastic test cell to the level of cell surface-expressed HSC70 in a non-neoplastic cell, wherein the test neoplastic cell is multidrug resistant or has multidrug resistance potential if the level of cell surface-expressed HSC70 in the test neoplastic cell is greater than the level of cell surface-expressed HSC70 in the non-neoplastic cell of the same origin or cell type.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification at Example 1 at page 98 lists parent cancer cell lines, its origin, and its counter part-MDR resistant cells, and also discloses examples 4-9 that the level of cell surface-expressed HSC70 in a number of MDR neoplastic cell lines originated from blood cancers and one breast cancer cells were higher than neoplastic cell lines, for example the HL60 cell line (page 108, lines 9-12), and normal blood cells do not express surface-expressed HSC70.

Gehrmann et al., Cell Stress Chaperones. 2005 June; 10(2): 136–146, teach that decrease in heat shock protein 70 membrane-positive tumor cells is observed in response to treatment of multiple drugs (see abstract), which is the opposite of the conclusion in the claimed invention. "In contrast to the cytosol, tumor cells with initially high Hsp70 membrane expression levels showed a significant reduction in Hsp70 membrane-positive cells after treatment with nontoxic doses of 13-RA and ATRA." Gehrmann et al., under the heading "DISCUSSION" teach that "Retinoids, synthetic derivatives of vitamin A, were frequently used in the therapy of premalignant and malignant cells, either alone or in combination with cytostatic drugs. Despite promising

results of ATRA in the redifferentiation of acute promyelocytic leukemia, intrinsic and acquired mechanisms of resistance to retinoids limit their therapeutic efficiency" and "Thyroid and colon cancer cells differ in their sensitivity toward direct toxic effects induced by 13-RA. For colon cancer cells a concentration of 10 μM and for thyroid cancer cells a concentration of 1 μM of 13-RA was found to be nontoxic." This teaching shows unpredictability of diagnosing MDR.

In addition, the specification does not give any indication whether the in vitro examples in the specification would be correlated in vivo, because the specification does not disclose any in vivo data, not even animal model.
Considering the unpredictable state of art, limited guidance with only in vitro cell lines with limited drug choice, no in vivo examples, broad breath of the claims, it is concluded that undue experimentation is required to practice the full scope of the claimed invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The applicable standard for the written description requirement can be found: MPEP 2163; University of California v. Eli Lilly, 43 USPQ2d 1398 at 1407; PTO Written Description Guidelines; Enzo Biochem Inc. v. Gen-Prove Inc., 63 USPQ2d 1609; Vas-

Cath Inc. v. Mahurkar, 19USPQ2d 1111; and University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC 2004).

The claims are interpreted as drawn to method of detecting a genus of proteins recited as "HSC70".

The specification at page 12 lines 17-18 discloses that "HSC70 polypeptide sequence having an amino acid sequence of SEQ ID NO:1", which is interpreted as the claimed HSC70 is a genus comprising any part of SEQ ID NO: 1" due to the indefinite article "an amino acid sequence" in front of "of SEQ ID NO:1" .

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is HSC70. There is not even identification of any particular portion of the structure that must be conserved in order to have the recited function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

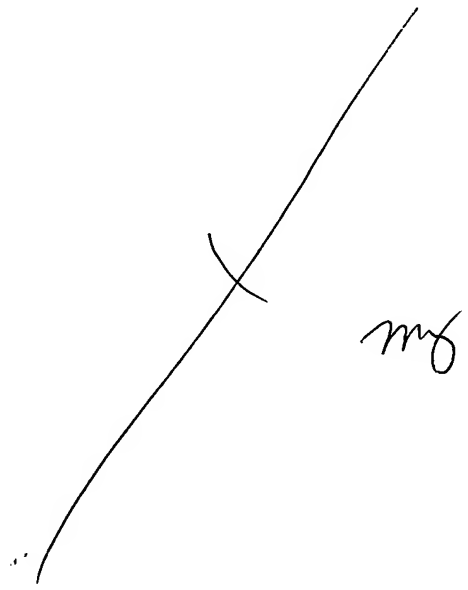
Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of protein molecules, given that the specification has only described SEQ ID NO: 1. Therefore, only isolated nucleic acid comprising SEQ ID NO:1, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MISOOK YU, Ph.D.
Primary Examiner
Art Unit 1642